patients with multiple myeloma (MM). Combining standard fractionated total body irradiation (TBI) with high-dose melphalan precludes optimal dosing of melphalan, and results in equivalent efficacy but more toxicity in comparison to high-dose melphalan (mel) alone. Helical tomotherapy is a novel tool for delivering CT image guided intensity modulated radiation therapy and may allow for greater doses of total marrow irradiation (TMI) and less collateral damage to other organs. We set out to test the feasibility of THDT inclusive of TMI. Eligible patients (≤70 years old, with stages I-III MM, in response or with stable disease, with a creatinine clearance of ≥50 mL/min) underwent mobilization with cyclophosphamide 1.5 gm/m^2 and G-CSF 10 microgram/kg and procurement of ≥ 4 × 10^6 CD34+ cells/kg. THDCT consisted of a set dose of mel 200 mg/m^2 followed by PBPC. At a minimum of 6 weeks later, TMI 200 cGy daily × 5 days, (to be escalated up to 200 cGy twice daily in a standard phase one cohort by cohort fashion) an PBPC is administered. Upon recovery, thalidomide 50–200 mg daily and dexamethasone 40 mg/day × 4 days every 28 days is to be prescribed. At dose level 1 (TMI: 200 cGy daily × 5 days) two patients (a 53 year old female with stage I MM in complete response and a 48 year old male with stage III MM in partial response prior to THDT) have completed THDT and are currently receiving maintenance. Neutrophyl and platelet recovery following TMI was observed by days 9 and 11, and platelet independence (defined as the day after the last platelet transfusion) was observed by day 10. Grade 1 emesis and grade 2 nausea, but no evidence of oral mucositis, enteritis, or skin erythema were noted. The estimated reduction in organ exposure to radiation with TBI versus TMI ranged from 6.5–6.9-fold (lens) to 2.5–2.6-fold (bowel), and 1.4–1.7-fold (lungs) in the first two patients treated. TMI is feasible for patients undergoing THDT for MM. Accrual is ongoing and results in patients treated at higher doses of TMI will be presented.

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COMPARISON OF CD34+ COLLECTIONS IN PATIENTS WITH MULTIPLE MYELOMA USING ETOPOSIDE/CYCLOPHOSPHAMIDE+GCSF, CYCLOPHOSPHAMIDE+GCSF, AND GCSF ALONE MOBILIZATION REGIMENS

Scott, L.M.[1], Brougher, L.I.[1], Anderson-Reitz, L.A.[1], Ensley, L.[1], Saracino, G.[1], Agura, E.D.[1], Berryman, R.B.[1], Fay, J.W.[1], Pineiro, L.[1], Vance, E.A.[1] [1]Baylor Sammons Cancer Center, Baylor University Medical Center, Dallas, TX.

Introduction: Low risk, curative therapy for patients with multiple myeloma remains elusive. Autologous stem cell transplant remains the standard of care for newly diagnosed multiple myeloma. Mobilization of adequate CD34+ cells can be a difficult task, especially in patients who have been heavily pretreated. We have compared the three mobilization regimens utilized at our facility and the subsequent CD34+ collections. **Background:** Standard chemotherapy is effective in maintaining control of multiple myeloma, however none has proven curative. Several trials have indicated that tandem or double autologous transplants may provide a significant benefit for overall survival and event free survival. When double transplants are planned, especially for patients who are heavily pretreated, collection of adequate CD34+ cells can prove to be challenging. **Methods:** 217 patients with multiple myeloma whose treatment plan included either a single or double autologous transplant were evaluated retrospectively. Data have been collected from January 1999 to March 2005. Mobilization regimens utilized were etoposide/cyclophosphamide+GCSF, 60 patients; cyclophosphamide+GCSF, 34 patients; and GCSF alone, 123 patients. Peripheral blood stem cells were collected following standard institutional procedures utilizing the Cobe Spectra apheresis machine. Standard CD34+ cell dose target for a single transplant was >2.0 × 10^6/kg. **Results:** Average and median CD34+ cell dose collected for patients receiving GCSF alone was 24.05 × 10^6/kg and 6.3 × 10^6/kg; cyclophosphamide+GCSF 13.28 × 10^6/kg and 9.75 × 10^6/kg; etoposide/cyclophosphamide+GCSF 39.98 × 10^6/kg and 30.4 × 10^6/kg. The average number of collections required for each regimen was 2.11 days for GCSF, 1.76 days for cyclophosphamide+GCSF, and 1.4 days for etoposide/cyclophosphamide+ GCSF. **Conclusions:** Etoposide/cyclophosphamide+GCSF mobilization regimen is highly effective in mobilizing large numbers of CD34+ cells in multiple myeloma patients making double or tandem transplants a viable treatment option.

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A PILOT STUDY OF CYCLOPHOSPHAMIDE, CARBOPLATIN, ETOPOSIDE (CCE), AND G-CSF WITH OR WITHOUT RITUXIMAB FOR CYTOREDUCTION AND PERIPHERAL BLOOD STEM CELL MOBILIZATION IN PATIENTS WITH RELAPSED OR REFRACTORY LYMPHOMAS

Stevenson, D.E.[1], Haroff, A.L.[1], Ririe, D.W.[1], Splichal, J.E.[1], Ornstein, D.L.[2], Heller, B.J.[3] 1. Wilford Hall Medical Center, Lackland AFB, TX; 2. University of Vermont/Fletcher Allen Health Care, Burlington, VT; 3. Malcolm Grow Medical Center, Andrews AFB, MD.

Background: Salvage chemotherapy is used for cytoreduction and PBSC mobilization in patients with relapsed and refractory lymphomas. Hospitalization is generally required for administration of the most commonly used regimens. We conducted a pilot study to determine the feasibility of delivering CCE with or without rituximab for cytoreduction and chemomobilization entirely in the outpatient setting to patients with refractory or recurrent non-Hodgkin's or Hodgkin's lymphoma who were candidates for high dose therapy with autologous stem cell support. **Methods:** 2 cycles of CCE were administered at 21 day intervals. The regimen consisted of cyclophosphamide 1 gram/m^2 on day 1, carboplatin at an AUC of 5 on day 2, and etoposide 100 mg/m^2 on days 1, 2, and 3. G-CSF, 5 mcg/kg/day was administered on days 5×12 with cycle 1 and the dose was increased to 10 mcg/kg/day for PBSC mobilization with cycle 2. After the first 8 patients, the protocol was amended to allow the use of rituximab at a dose of 375 mg/m^{2}on days 1, 8, and 15 of each cycle for those patients with CD20+ lymphomas. **Results:** 18 patients have been enrolled and have completed CCE. The diagnoses include B-cell non-Hodgkin's lymphoma (B-NHL; n = 8 large cell, n = 2 follicular), Hodgkin's lymphoma (n = 3), peripheral T-cell lymphoma (n = 2), anaplastic large cell lymphoma (n = 1), composite B-NHL/Hodgkin's lymphoma (n = 1), and T-cell rich, B-cell lymphoma (n = 1). The median age was 46 years (range 19–69). One patient received one cycle of CCE, while 2 patients received more than 2 cycles. The overall response rate for the regimen is 63% (3 CR, 7 PR, 5 SD, 1 PD, 2 not evaluable). PBSC were collected successfully from 16/18 patients. The median number of PBSC collected was 7.5 × 10^6 CD34+ cells/kg (range 2.1–16.8 × 10^6), and the median number of apheresis sessions was 2 (range 1–9). There were 4 hospitalizations for neutropenic fever in 38 cycles. Non-hematologic toxicity was minimal, and no deaths occurred on study. All patients from whom sufficient PBSC were collected underwent high dose therapy with autologous PBSC rescue, and hematologic recovery occurred in 100%. **Conclusions:** The interim results of this pilot study suggest that CCE is a safe and effective outpatient regimen for cytoreduction and PBSC mobilization for relapsed or refractory non-Hodgkin's and Hodgkin's lymphoma. This regimen warrants further study, and a total of 30 patients will be enrolled on this continuing study.

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SALVAGE AUTOLOGOUS TRANSPLANTATION IN MULTIPLE MYELOMA

Qazilbash, M.H.[1], Saliba, R.[1], Mendoza, F.[1], Roden, L.[1], Hosing, C.[1], Couriel, D.[1], Kebriaei, P.[1], Popat, U., DeLima, M.[1], Champlin, R.E.[1], Giralt, S.A.[1] [1]University of Texas-M. D. Anderson Cancer Center, Houston, TX.

Introduction: Most patients undergoing high-dose therapy and autologous transplant for multiple myeloma eventually relapse. The optimal treatment for these patients is still evolving. There have been few reports of autologous transplants in the salvage setting. We analyzed the outcome of salvage autologous transplant in 22 patients with disease progression after the first autograft. **Methods:** These patients in general were not eligible for an allo-

geneic transplant due to older age, comorbidities or lack of HLA-identical donor. Median age at transplant was 52 years (range 37–68), median interval between first and second autograft was 26 months (range 3–73). Eleven patients had persistent or progressive disease at transplant. Twenty patients received high-dose melphalan alone or in combination, while 2 received a combination of thiotepa, busulfan and cyclophosphamide. Patients had received an average of 6 prior chemotherapy regimens. Cytogenetic studies were available in 18/22 patients at the time of transplant, 12 were normal and 6 abnormal. **Results:** 14 of the 21 evaluable patients (70%) achieved a response (1 CR, 13 PR). After a median follow-up of 15 months (2–82), 1 year progression-free survival (PFS) was 40% and 1-year overall survival (OS) was 78%. 100-day TRM was 0%. Median PFS was 10 months, and median OS has not been reached. On univariate analysis, abnormal cytogenetics at transplant was a predictor of shorter overall survival ($P = .01$). **Conclusions:** In patients with progressive disease after an autologous transplant, salvage autologous transplants may achieve responses in 70% of patients with durable remissions in a small subset. Normal cytogenetics at second transplant predicts a longer survival.

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AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN MULTIPLE MYELOMA USING MELPHALAN: THE MEXICAN EXPERIENCE

Vela-Ojeda, J.[1], Garcia-Ruiz Esparza, M.[1], Padilla-Gonzalez, Y.[1], Ruiz-Argüelles, G.J.[2], Gomez-Almaguer, D.[3], Delgado-Lamas, J.L.[4], Gomez-Rangel, J.D.[3], Morales-Toquero, A.[2], Ruiz-Delgado, G.J.[2] 1. UMAE Hospital de Especialidades Centro Médico La Raza, IMSS, Mexico, DF, Mexico; 2. Centro de Hematología y Medicina Interna de Puebla, Puebla, Mexico; 3. Hospital Universitario de Nuevo León, Monterrey, Nuevo Leon, Mexico; 4. UMAE Hospital de Especialidades Centro Médico de Occidente, IMSS, Guadalajara, Jalisco, Mexico.

Background: Autologous peripheral blood stem cell transplantation is at the present the therapy of choice for the treatment of multiple myeloma (MM) patients younger than 70 years old. **Methods:** Between August 1993 and November 2004, fifty four patients with MM were autografted; median age was 49 years (range 20–69). Patients were given a median of 4.3×10^6/Kg CD34 (+) viable MNC after conditioning with high-dose melphalan regimens (oral or I.V. in 47 and 7 patients, respectively). **Results:** Median time to achieve $> 0.5 \times 10^9$/L granulocytes was 12 days, whereas median time to achieve $>20 \times 10^9$/L platelets was 15 days. Thirty seven patients are alive 15 to 157 months after the autograft (median 86 months). The 7-year disease-free and overall post-transplant survival is 24% and 60%, respectively. The transplant-related mortality was 13%. Seven patients died as a result of the toxicity of the conditioning regimen, whereas death in the remaining 10 cases was related to post-transplant relapse of the malignancy. Four good-prognostic factors were identified: interval between diagnosis and transplant less than 24 months, number of prior chemotherapy regimens <2, remission status (complete or partial), and pretransplant β2microglobulin less than 3 mg/dL. **Conclusions:** Autologous peripheral blood stem cell transplantation using oral melphalan was a good choice of treatment for Mexican multiple myeloma patients. Transplant-related mortality was higher in comparison with other studies.

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DRAMATIC IMPROVEMENT OF POEMS SYNDROME BY STEM CELL TRANSPLANTATION PARALLELS DECREASE IN VEGF AND BFGF LEVEL

Schrader, C.[1], Tiemann, M.[2], Zirrgiebel, U.[3], Günther, A.[1], Janssen, D.[4], Gramatzki, M.[1] 1. [1]2nd Department of Medicine, University of Kiel, Kiel, Germany; 2. [2]Department of Hematopathology, Hamburg, Germany; 3. [3]Proqinase GmbH, Freiburg, Germany; 4. [4]Department of Hematopathology and Lymph Node Registry, Kiel, Germany.

Purpose: POEMS syndrome is a rare disease characterized by polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes. We treated a severely ill woman with a 4-year history of polyneuropathy showing all signs of a POEMS syndrome. Response to chemotherapy including high-dose melphalan treatment and autologous stem cell transplantation was monitored and vascular endothelial growth factor (VEGF) as well as basic fibroblast growth factor (bFGF) levels were measured. **Methods:** Blood investigation was done for serum electrophoresis analysis and analysis of VEGF, bFGF, and IL-6 by ELISA. Bone marrow biopsy specimen was investigated immunohistochemically for IgA, IgG, kappa, lambda, CD20, CD56, cyclin D1, and VEGF. **Results:** Immunohistochemical investigation of the bone marrow biopsy showed an infiltration of IgA and lambda positive plasma cells (10%). Only few plasma cells expressed kappa. The tumor cell were negative for CD20, CD56, and cyclin D1, but positive for VEGF in line with the high VEGF levels in the blood. Blood investigation revealed a discrete monoclonal gammopathy of IgA lambda type. Initially, high level of VEGF (1468.7 pg/ml) and bFGF (112.9 pg/ml) were detected. However, treatment with high-dose melphalan and tandem autologous stem cell transplantation proved extremely helpful in disease control. Already after the first transplant the patient started again walking and lost her pulmonary hypertension. In parallel VEGF and bFGF levels decreased and the performance status of the patient improved dramatically. **Conclusions:** VEGF and bFGF measurement is a useful tool for monitoring disease activity in POEMS syndrome. Moreover, although stem cell transplantation is of utmost importance even in patients with severely reduced performance status, these pathophysiologic findings may provide a rational for additional treatment approaches with anti-angiogenetic substances.

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BONE MARROW TRANSPLANTATION FROM MATCHED UNRELATED DONORS FOR PATIENTS WITH SEVERE COMBINED IMMUNE DEFICIENCY

Grunebaum, E.[1], Atkinson, A.R.[1], Reid, B.[1], Roifman, C.M.[1] [1]Hospital for Sick Children, Toronto, ON, Canada.

Introduction: Bone Marrow Transplant (BMT) from related HLA identical donor (RID) is the treatment of choice for patients with severe combined immuno-deficiency (SCID). In the absence of RID, bone marrow from HLA haplo-identical (half) related donors (HID) have often been used. However, HID is frequently associated with reduced survival and failure of long-term immune reconstitution. HLA matched unrelated donors (MUD) represent another promising alternative for patients with SCID. **Methods:** We studied hematopoietic engraftment, occurrence of graft versus host disease, infections and other complication, and survival in infants diagnosed with SCID who received MUD BMT between 1990 and 2004 in a Canadian pediatric referral center specializing in such procedures. Detailed evaluations of immune reconstitution were performed in children that survived more than 2 years after transplant. **Results:** During the 14 years of this study, 22 infants underwent MUD BMT in our center. Molecular diagnosis was available in 64% of them. All infants received myelo-ablative conditioning pre-transplant. Despite prophylaxis with cyclosporine and methylprednisolone, acute graft versus host disease occurred in 15 of the 22 patients, and it was the most common cause of death. All patients developed complete donor lymphocyte engraftment. None of the 15 patients who are two or more years after transplant requires intravenous immunoglobulin replacement therapy. After discontinuing immune suppression all patients have normal T cell function and T cell repertoire, which is sustained for more than 14 years of follow up. Current survival is 73% and it is even better for patients with mutations in the IL-2 receptor pathway. Furthermore, survival of patients who presented with low B cells, previously estimated to have unfavorable outcome, is not significantly lower than in other forms of SCID in this study. **Conclusions:** MUD BMT leads to long term survival, engraftment, and immune function in SCID patients and should be the preferred treatment for clinically stable infants who do not have a related HLA-identical donor.